Kuskokwim syndrome

Kuskokwim syndrome is characterized by joint deformities called contractures that restrict the movement of affected joints. This condition has been found only in a population of native Alaskans known as Yup'ik Eskimos, who live in and around a region of southwest Alaska known as the Kuskokwim River Delta.

In Kuskokwim syndrome, contractures most commonly affect the knees, ankles, and elbows, although other joints, particularly of the lower body, can be affected. The contractures are usually present at birth and worsen during childhood. They tend to stabilize after childhood, and they remain throughout life.

Some individuals with this condition have other bone abnormalities, most commonly affecting the spine, pelvis, and feet. Affected individuals can develop an inward curve of the lower back (lordosis), a spine that curves to the side (scoliosis), wedge-shaped spinal bones, or an abnormality of the collarbones (clavicles) described as clubbing. Affected individuals are typically shorter than their peers and they may have an abnormally large head (macrocephaly).

Frequency

Kuskokwim syndrome is extremely rare. It affects a small number of people from the Yup'ik Eskimo population in southwest Alaska.

Genetic Changes

Kuskokwim syndrome is caused by mutations in the *FKBP10* gene, which provides instructions for making the FKBP10 protein (formerly known as FKBP65). This protein is important for the correct processing of complex molecules called collagens, which provide structure and strength to connective tissues that support the body's bones, joints, and organs. Collagen molecules are cross-linked to one another to form long, thin fibrils, which are found in the spaces around cells (the extracellular matrix). The formation of cross-links results in very strong collagen fibrils. The FKBP10 protein attaches to collagens and plays a role in their cross-linking.

A mutation in the *FKBP10* gene alters the FKBP10 protein, making it unstable and easily broken down. As a result, people with Kuskokwim syndrome have only about 5 percent of the normal amount of FKBP10 protein. This reduction in protein levels impairs collagen cross-linking and leads to a disorganized network of collagen molecules. It is unclear how these changes in the collagen matrix are involved in the development of joint contractures and other abnormalities in people with Kuskokwim syndrome.

Inheritance Pattern

This condition is inherited in an autosomal recessive pattern, which means both copies of the gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of the mutated gene, but they typically do not show signs and symptoms of the condition.

Other Names for This Condition

- arthrogryposis-like syndrome
- Bruck syndrome 1
- Kuskokwim disease

Diagnosis & Management

These resources address the diagnosis or management of Kuskokwim syndrome:

- Genetic Testing Registry: Bruck syndrome 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1850168/

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Contracture Deformity
  https://medlineplus.gov/ency/article/003185.htm
- Health Topic: Joint Disorders
  https://medlineplus.gov/jointdisorders.html

Genetic and Rare Diseases Information Center

- Kuskokwim disease
  https://rarediseases.info.nih.gov/diseases/3150/kuskokwim-disease

Educational Resources

- Disease InfoSearch: Kuskokwim disease
  http://www.diseaseinfosearch.org/Kuskokwim+disease/4053
- MalaCards: bruck syndrome 1
  http://www.malacards.org/card/bruck_syndrome_1
- Orphanet: Arthrogryposis-like syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1149

Patient Support and Advocacy Resources

- Resource List from the University of Kansas Medical Center: Arthrogryposis
  http://www.kumc.edu/gec/support/arthrogr.html

Genetic Testing Registry

- Bruck syndrome 1
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C1850168/

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Kuskokwim+syndrome%22+OR+%22Arthrogryposis%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28kuskokwim+syndrome%29+AND+english%5Bla%5D

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